201-15754

The Dow Chemical Company
Midland, Michigan 48674

20 December 2004

Mr Michael O. Leavitt, Administrator
US Environmental Protection Agency
P.O.Box 1473
Merrifield, VA 22116

The Dow Chemical Company thanks the Environmental Protection Agency and Environmental Defense for reviewing and commenting on the draft test plan and dossier for chloromethyl methyl ether (CMME) (CAS# 107-30-2). The Dow Chemical Company has been unable to form a consortia and has subsequently updated the test plan providing information on exposure and use of CMME within The Dow Chemical Company. The test plan and dossier have also incorporated comments made by EPA and Environmental Defense.

Response to Environmental Defense comments.

- We do ask the sponsor, in the revised submission, to provide a summary of the histological methods used in the repeat dose and cancer studies.
    - Whenever possible, this information has been added to the dossier.

- The test plan indicates that no reproductive or developmental studies are available on CMME, but the sponsor does not indicate whether or not such studies will be performed.
    - Several points have been added to the test plan and we will restate them here. Since this material is a chemical intermediate, a reproduction study is unnecessary. Since the material has a high vapor pressure, the most likely route of exposure is via the inhalation route. Any inhaled CMME would hydrolyze rapidly in the respiratory tract or in the blood stream. CMME hydrolyses extremely rapidly in water (half life <0.007 seconds) breaking down to HCl, formaldehyde and methanol. Although these materials can recombine or rearrange to form bis chloromethylether at high concentrations, the low concentrations present in the blood stream would preclude that from happening. Thus, CMME would break down prior to reaching the fetus. Robust summaries of developmental studies on the breakdown products have been added to the dossier.
- It would be helpful also to provide information on reproductive tract histology from interim sacrifices, if available, from the cancer studies.
    - The repeat and cancer studies did not examine reproductive tract histology.

- The test plan also notes that no data are available for the ecological toxicity endpoints: toxicity to fish, aquatic invertebrates and algae. The sponsor contends that these studies are not needed because CMME is highly reactive and rapidly hydrolyzed. The degradation products include formaldehyde, methanol and hydrochloric acid, and all of these have data for the three ecological toxicity endpoints. If formaldehyde, methanol and hydrochloric acid constitute the great majority (e.g., at least 90%) of the total hydrolysis products, then we can agree with the sponsor. If other degradation products occur in significant amounts and are not themselves derived from formaldehyde, methanol or hydrochloric acid, then it may be necessary to conduct the aquatic toxicity tests. Therefore, we request that additional information on hydrolysis/degradation products be provided in the revised test plan submission.
    - When CMME breaks down via hydrolysis, formaldehyde, methanol and hydrochloric acid are the only known breakdown products.
- Are monitoring data available which (hopefully) demonstrate that workplace levels are consistently below 1 ppb?
    - Exposure data has been added to the test plan. Occupational exposure limits of 100 ppb for CMME (Dow Industrial Hygiene Guideline) and 1 ppb for bis chloromethylether (ACGIH TLV) have been set. A review of full-shift and short term monitoring data (1981 to current) for potential exposure to CMME and BCME indicate that potential exposures are below established exposure guidelines.
- The test plan summary on in vitro mutagenicity is inconsistent with the information provided in the robust summaries.
    - This has been updated.
- Are the same degradation products formed in air as in water, but at a slower rate in air?
    - The same degradation products would be formed via hydrolysis. In the vapor phase at 25C and 70% relative humidity, the half life for 100 ppm and 1000 ppm CMME is 6 minutes and 3.5 minutes, respectively, Degradation via photodegradation through hydroxyl radicals occurs at a slower rate and has been calculated to take as long as 4 days. Intermediate compounds formed are methyl formate and chloromethylformate. These ultimately degrade to formaldehyde, HCl and carbon dioxide.
- Are the degradation products responsible for the carcinogenicity of CMME following inhalation exposures, and/or is the inherent reactivity of CMME the primary mode of action?
    - The inherent reactivity of CMME and/or BCME is believed the primary mode of action.
- There are several other typographical errors that need to be corrected in the revised submission.
    - The document has been reviewed.

Response to EPA comments.

- General. The submitter needs to complete the test plan as the original submitter or as part of a consortium as discussed in the submission cover letter

    - The Dow Chemical Company has been unable to form a consortia and is proceeding alone and, as such, has completed the test plan.
- Physicochemical Properties and Environmental Fate. A robust summary needs to be provided for fugacity.
    - A Mackay Level III fugacity model has been added to the dossier.
- Health Effects. The submitter needs to explain why reproductive and developmental toxicity data are not needed or are not being addressed now because of the effort to form a consortium to address these endpoints.
    - Several points have been added to the test plan and we will restate them here. Since this material is a chemical intermediate, a reproduction study is unnecessary. Since the material has a high vapor pressure, the most likely route of exposure is via the inhalation route. Any inhaled CMME would hydrolyze rapidly in the respiratory tract or in the blood stream. CMME hydrolyses extremely rapidly in water (half life <0.007 seconds) breaking down to HCl, formaldehyde and methanol. Although these materials can recombine or rearrange to form bis chloromethylether at high concentrations, the low concentrations present in the blood stream would preclude that from happening. Thus, CMME would break down prior to reaching the fetus. Robust summaries of developmental studies on the breakdown products have been added to the dossier.
- Ecological Effects. Robust summaries are needed for the hydrolysis products for each endpoint indicating that toxicity will be equivalent to the product with the highest toxicity, i.e., formaldehyde.
    - Robust summaries have been added to the dossier.

Sincerely,

Kenneth D. Nitschke, D.A.B.T.
The Dow Chemical Company
1803 Bldg
Midland, MI 48674